STEM CELLS TRANSLATIONAL MEDICINE®

MEETING REPORT

Report of the International Stem Cell Banking Initiative Workshop Activity: Current Hurdles and Progress in Seed-Stock Banking of Human Pluripotent Stem Cells

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ABSTRACT

This article summarizes the recent activity of the International Stem Cell Banking Initiative (ISCBI) held at the California Institute for Regenerative Medicine (CIRM) in California (June 26, 2016) and the Korean National Institutes for Health in Korea (October 19–20, 2016). Through the workshops, ISCBI is endeavoring to support a new paradigm for human medicine using pluripotent stem cells (hPSC) for cell therapies. Priority considerations for ISCBI include ensuring the safety and efficacy of a final cell therapy product and quality assured source materials, such as stem cells and primary donor cells. To these ends, ISCBI aims to promote global harmonization on quality and safety control of stem cells for research and the development of starting materials for cell therapies, with regular workshops involving hPSC banking centers, biologists, and regulatory bodies. Here, we provide a brief overview of two such recent activities, with summaries of key issues raised. STEM CELLS TRANSLATIONAL MEDICINE *2017;6:1956–1962*

SIGNIFICANCE STATEMENT

This article reviews recent discussions among world leading groups working on the provision of stem cell lines for research and clinical use. It addresses the latest thinking on issues of quality control, safety, and ethics. A key outcome from the reported workshops was the confirmation of the need for standards and, in particular, the principles of best practice which have been developed by the International Stem Cell Banking Initiative.

INTRODUCTION

International Stem Cell Banking Initiative (ISCBI) was established in 2007 with funding from the International Stem Cell Forum (http://www.stem-cell-forum.net/), with the remit to support human pluripotent stem cells (hPSC) banking centers, stem cell biologists, regulatory bodies, and others involved and/or interested in biobanking [1–3]. The ISCBI members have held regular workshops and have published a series of publications including best practice for the preparation and dissemination of hPSCs for research and clinical application [4, 5]. The ISCBI meetings regularly

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involved delegates from up to 24 countries to reach consensus on core standards for the field of stem cell research and development. In 2016, the ISCBI held a meeting in California (CiRM, 26th June) and a workshop at the Korean National Institutes for Health (KNIH) in Korea (19–20 October). In this Report, we provide a summary of the key points of discussion from both meetings, with emphasis on data standardization, quality controls for quality assurance, resource sharing, and the tenet of informed consent.

Data Standardization, Protection

The hPSCreg Project

Prof. Andreas Kurtz (Charité Universitätsmedizin, Berlin, Germany) reported on the hPSCreg database funded by the European Commission (EC), which now contained information on about 1,600 hPSC lines from 26 countries. The EC requires registration and certification of all human embryonic stem cell (hESC) and hiPSC lines by the registry before they can be used for EC-funded research, which involves validation of ethical provenance, identity and evidence of pluripotency. A more convenient facility for registering cell lines in batches is available for cooperation partners. hPSCreg adopts provisions to protect donor privacy. For instance, certain cell line's genetic and clinical data sets, which might be misused to reidentify anonymized donors, for example, human leukocyte antigen (HLA) and short tandem repeat (STR) profiles, genetic sequences, are held on the database, but are not released publicly if open access was not granted by the consenting donor [6]. The registry makes only two alleles of a STR profile available for public access, which would enable researchers to initiate independent confirmation of cell authenticity without releasing full STR profiles. Delegates supported the need for a standardized nomenclature for cell naming as published by International Stem Cell Initiative (ISCI) contributors [7], which also included a recommendation on minimal information to be included in publications of new hPSC lines. hPSCreg has implemented an automated tool and register for naming of hPSC lines according to a modification of the nomenclature standard [8] (https://hpscreg.eu/). It was acknowledged that day-to-day use of simplified local names was likely to continue for convenience; but it was felt timely to try to persuade scientists to use a standard nomenclature for formal identification, reporting, and referencing of cell lines.

Development of Minimum Information Guidelines for Stem Cell Data

Prof. Wataru Fujibuchi (Center for iPS Cell Research and Application, Kyoto University, Japan) described the MIACARM (Minimum Information About a Cellular Assay for Regenerative Medicine), which was published by an international team including Europe, Japan, and the U.S. in October 2016 [9]. He described the MIACARM data ontogeny which was designed to help standardize capture of scientific data and processing information applicable to most stem cell banks and cellular information registries. This was intended to promote data exchange and facilitation of practical regenerative medicine. He also outlined the early development of a standardized ontogeny of cell/tissue descriptors. He indicated that he was keen to develop and improve the system and requested feedback on the proposed ontogeny from ISCBI members via completion of a "cross-referencing template" and application programming interface (API). (http://icscb.stemcellinformatics.org).

Data Access for Human Induced Pluripotent Stem Cell (hiPSC) Lines

Laura Clarke (EMBL-EBI, Cambridge, U.K.) described the role of the European Genome-Phenome Archive [10] in providing access to biological data via a range of data access arrangements for different cohorts of sample donors. The archive contains sequence, array, and phenotypic data, with access to data controlled by the submitter. She also described the HipSci project [10] which had created 719 induced pluripotent stem cell (iPSC) lines (156 then available from European Collection of Authenticated Cell Cultures (ECACC) a member of the EBiSC European iPSC bank project). She explained the need for care in the management of "unique data" which she defined as pieces of data which could be used in combination with other data sets to reidentify an individual. Sequence data were the prime example of such unique data while proteomics data were considered to be unlikely to facilitate reidentification of donors. She also outlined the role of the Global Alliance for Genomics and Health in providing strategic coordination for the management of such data sets.

National and International Stem Cell Banking Activities

The importance of well-documented quality control and rigorous traceability for donor materials and the banking process were consistent features in presentations by stem cell banking centers from Asia, Europe, and North America (see Table 1) who endorsed the use of international consensus for stem cell banking [5]. In addition, it was also concluded that retention of original cells used to prepare iPSC lines was crucial to enable new lines to be developed as iPSC technology advanced and to provide archival material for testing in the event of infections or other adverse events in iPSC clinical trials.

Dr. Joanne Mountford (Scottish National Blood Transfusion Service, Edinburgh, U.K.) described the formation of a global HLA homozygous haplobank consortium [11] aimed to provide tissue type matched therapies with reduced risk of immune rejection in patients. She explained that the development of autologous cell lines was prohibitively expensive for widespread use but a key regulatory challenge also remained to realizing products from a panel of such lines which was the ability to demonstrate comparability between products made with different iPSC lines. It was also agreed that at this point in time it is not clear which reprogramming methods will prove most satisfactory. Accordingly, it was considered important to ensure that stocks of cryopreserved donor fibroblast cultures or primary cells/tissues are retained so that when more advanced reprogramming techniques are available new iPSC lines can be derived from the most valuable donor genotypes.

Prof. Tsuneo Takahashi (University of Kyoto, Japan) described the Japanese Cord Blood Bank Network established in 1998. The network primarily supported by the Japanese Red Cross had a program that treated more than 1,000 patients per year using unrelated cord blood. This was linked with the Japan Marrow Donor Program (JMDP), which has registered over 400,000 donors. He also described the provision of cord blood units for research purposes from the Riken BioResource Center in Tsukuba City. Prof. Takahashi proposed that the basic protocols to produce clinical grade stem cells should be harmonized and the developing regulations for regenerative medicine and was convinced that international guidance, like those of the ISCBI [5], is critical for the progress of the development of other tissue materials used for cell therapy and regenerative medicine.

Table 1. National stem cell banking and resource sharing

		Center	Available cell lines	Information	Governance/Funding
Asia	India	JNCASR http://www.jncasr.ac.in/inamdar	hESC	Eight hESC lines are available. Two lines are deposited to UKSCB (see above)	Government funded
	Japan	CiRA http://www.cira.kyoto-u.ac.jp/	hiPSC, mESC	Non-for profit and profit materials are available: human iPSCs, Diseases iPSCs, mouse iPSC and ES cells	Government funded
	Korea	KSCB (KNIH) http://kscr.nih.go.kr/	hESC, iPSC, GMP grade iPSC banking and registry	The Korea government embryonic stem cell registry. Current status: 128 hESCs. Banking: 18 GMP grade homozygote HLA iPSC lines are deposited	Government funded
	Singapore	SSCB (IMB) https://www.a-star.edu.sg/imb/tech-platforms/cell-banks	iPSC	The SSCB is a centralized repository and distributor of iPSC. The bank also provides technical support and educational opportunities through hands on training	A-Star funded
	Thailand	TSCB	hESC, iPSC	iPSCs from the patients such as Wiskott-Aldrich syndrome, Osteoimperfecta, Alzheimer's and Thalassemia disease are established	University
Europe	Europe	EBiSC http://www.ebisc.org	iPSC	iPSCs from disease affected donors and relatives (neurodegenerative, eye, heart) and healthy controls	European Commission-private partnership partnership project (IMI/EFPIA)
	France	I-Stem http://www.istem.eu/	hESC, iPSC	The largest French laboratory dedicated to hiPSC, embryonic origin or obtained by reprogramming gene	Government-private collaboration
	U.K.	HiPSCi http://www.hipsci.org/	iPSC, disease cohort, data	Systematically generating iPSCs from hundreds of donors and banked at EBiSC	Government funded
	Germany	hPSCreg https://hpscreg.eu/	hESC, iPSC registry	Global registry for human pluripotent stem cell lines (hPSC lines). Current status: 706 hESC lines and 523 iPSC lines	European Commission funding
	Spain	Spanish National Stem Cell Bank	hESC, iPSC	National Spanish Registry of Stem Cell Lines hESC for clinical and research use, hiPSC for research	Government funded (Institute Carlos IIII)
	U.K.	UKSCB http://www.nibsc.org/	hESC, hiPSC, GMP grade hESC	Panel of 38 new clinical grade hESC lines derived and banked specifically for clinical application under EU regulations and according to the ISCBI guidance	Government funded
North America	U.S.	Coriell/CDI https://cellulardynamics.com/	iPSC	Currently establishing banks of 3,000 lines	Californian Institute for Regenerative Medicine
	U.S.	NYSCF nyscf.org/	iPSC	Diseases specific iPSC panels	Not-for-profit company
	U.S.	RUCDR rucdr.org/	iPSC, GMP grade iPSC	Maintains Stem Cell Resource for the NIMH https://www.nimhgenetics.org/stem_cells/, the NINDS. Distributes cGMP grade iPSC lines, control and reporter lines for the NIH Regenerative Medicine Program (RMP)	Government funded
	U.S.	WiCell //http://www.wicell.org	hESC, hiPSC, GMP grade hESC	1,200+ research grade cell lines available including disease models and controls. H1 (WA01), H9 (WA09), and H14 (WA14) cell line banked under GMP conditions and the matched research bank materials are available	Not-for-profit company

Abbreviations: ES, embryonic stem cell; EU, European Union; GMP, good manufacturing practice; hESC, human embryonic stem cell; hiPSC, human induced pluripotent stem cell; iPSC, induced pluripotent stem cell; mESC, mouse embryonic stem cell.

Quality Control Focused on Genetic Stability Testing

Characterization of a CIRM-Funded iPSC Resource

Dr. Thomas J. Novak (Cellular Dynamics International, Wisconsin, U.S.) described Cellular Dynamics International (CDI's) work to bank and quality control the 3,000 hPSC lines derived from blood (80%) and skin (20%) cells using episomal reprogramming, under sponsorship from CIRM. A total of 1,000 lines deposited at Coriell had been characterized by a range of methods. A 300,000 SNP genome array (Illumina's Infinium HumanCore SNP-Chip) was used to evaluate genome status which was broadly equivalent in resolution to G-banding and, in addition, revealed insertion and deletions (in/dels). SNP-Chip had facilitated high throughput and low-cost analysis, but this had to be balanced against a compromise on inability to detect inversions and reciprocal translocations. Differences between karyotype and genome array data had been observed and the array analysis had missed certain cytogenetic changes, but gives some potentially valuable genomic data on specific sequences affected. Multiple clones from the same individuals had been generated, but budgetary constraints prevent more than one clone from being analyzed. So far approximately 20% of lines did not meet the requirements for karyotype acceptability and Dr. Novak reported that full analysis of the data would be released in 2018–2019 once it has been analyzed by awardees of CIRM grants to establish the lines. In the meantime, individual grant recipients could be approached for the data on their own lines.

Genetic Stability in Cell Lines in Routine Banking of hPSC Lines at WiCell

Dr. Tenneille Ludwig (WiCell, U.S.) moderated a discussion on common recurrent abnormalities seen in human pluripotent stem cell banking. Group discussion highlighted the apparent trends in the appearance of abnormalities, including the previously reported amplicon in chromosome 20 [12]. The discussion highlighted the prevalence of specific abnormalities across laboratories globally and underscored the need for testing strategies and tools to identify these recurrent abnormalities in routine culture and banking.

Genetic Studies of hESC Banks at the KNIH

Dr. Jung-Hyun Kim (Korea National Stem Cell Bank, KNIH, South Korea) reported in depth genetic characterization of the first K-NIH hPSC lines. Data included analysis of copy number variation (by whole exome sequencing, array comparative genomic hybridization (aCGH), and array single nucleotide polymorphism (aSNP)), RNAseq, and epigenetic profiles. Parallel analysis of samples from premaster, master, and distribution cell banks for each of the six lines had revealed only one change in karyotype in DNA chromosomal analysis between cell banks of the same line.

Comparison of Alternative Methods for the Evaluation of Genetic Stability in the EBiSC Project

Dr. O'Shea (UK Stem Cell Bank, NIBSC, South Mimms, U.K.) described a project initiated within the European iPSC bank (EBiSC) which had performed a comparison of three techniques for assessment of genome integrity (Geimsa-banded karyotype, Bacs on Beads ["BoBs"] and arraySNPs) from common cell line samples. Data to date indicated that BoBs missed a significant proportion of genetic changes observed with the other two methods, possibly due to its lower sensitivity. G-banding had detected some changes not seen in a SNP analysis but also aSNPs had detected quite large deletions not seen in karyology. Identical samples of one cell line sent to three independent cytogenetic laboratories also showed variation in detailed G-banded karyotype and the relative proportions of altered clones. The results yet to be fully completed, raised questions including: what do the observed changes and variations mean, what level of cells with abnormal karyotype would classify a cell line as atypical, should banks be using a combination of techniques, and how should such genetic stability data be published by stem cell banks.

QC Test Package Required for iPSC Banks for Clinical Use Established at the Foundation for Biomedical Research and Innovation

Prof. Shin Kawamata (Foundation for Biomedical Research and Innovation [FBRI], Kobe, Japan) introduced the QC test requirements for the iPSC-derived product at clinical sites and iPSC clinical banks, based on the experience of the clinical application of autologous and allogenic iPSC derived retinal pigmented epithelium in Kobe. He mentioned that the iPSC generated by reprogramming should be carefully checked for differentiation capability because retention of reprogramming factors, genetic damage during reprogramming, or the presence of abnormal epigenetic modification which can render certain differentiation protocols ineffective. These were considered important in addition to genetic changes accumulated in the course of long-term culture of PSC which could generate tumor populations after transplantation. He proposed distinct QC test sets for iPSC-derived products at clinical sites. The in vivo transplantation test of the differentiated final product to address tumorigenic and differentiation potential by examining histology of transplant can also be included. In addition, a set of simple genetic tests such as karyotyping, CGH array can be considered depending on the nature of the product. The purpose of QC tests at the clinical site is to provide enough information for a go/no go decision by the clinical investigator. Therefore, whole genome sequence data in clinical grade iPSC cell bank without any clinical information may not be relevant as it is not useful for this kind of decision. He also addressed the importance of coordination between the iPSC bank and clinical sites using the iPSCs, to share data on in vivo QC testing of iPSC-derived differentiated cells and QC tests of original iPSC clones. The QC data sharing system in the community would also contribute to improve the quality of iPSC clones in the bank and consequently promote iPSC-derived cell therapy.

The Quality Control (QC) Requirements and Evaluation of Nonpluripotent Stem Cells

Dr. Bao-Zhu Yuan (NIFDC, Beijing, People's Republic of China) introduced a quality control system established by the National Institutes for Food and Drug Control, an integral part of China FDA. A key part of this system is the "quality evaluation system," designed for the evaluation of mesenchymal stromal cells during preclinical product development. To assure the quality of the cells to be used in humans in the so-called "clinical studies," the cells were expected to meet the quality requirements of four major categories, which are the general biological properties, microbiology safety, biology safety, and biological effectiveness. The process is performed under a quality management system, which determines the evaluation

strategies, in which different assessment techniques are combined, according to type, manufacturing process, and clinical indication of different cells. Another key component was the quality evaluation technology system, which is a collection of quality assessment technologies used to evaluate various critical quality attributes within each category of the major quality requirements. By applying the evaluation system, several common quality issues had been identified among the different products assessed up to the date of the meeting including the problems associated with cell identity, purity, mycoplasma contamination, and significant variations in biological activity. Although the new system had been focused on stem cells, it was believed that its principles are also applicable to all other therapeutic cells, including immunotherapeutic cells.

Stem Cell Characterization

A UV-Lithography Surface Patterning Process for Cell Differentiation

At the 2015 ISCI/ISCBI meeting, Nafees Rahman (University of Toronto, Canada) had described a 48-hour induced differentiation assay which used assessment of Oct4/Sox2 expression to distinguish undifferentiated cells from neuroectoderm, primitive streak, and extraembryonic differentiated cultures [13]. She subsequently reported (ISCBI workshop June 2016) a development of this assay using UV-lithography for surface patterning. This development enabled creation of different patterns of surface treatment shown in the presentation, which could be used to influence cell differentiation in different ways. Gastrulation-like differentiation had been modeled using this system using defined media and was being investigated with a broader range of cell lines. The assay was being developed to investigate the effect of bioactive molecules such as kinase inhibitors. The technology had now developed to the stage where the treated surfaces could be distributed to other labs thus facilitating more wider use of this system [14].

New Developments for the Pluritest Assay

Dr. Jeanne Loring (Scripps Research Institute, LaJolla, U.S.) described the success of uptake of Pluritest, with 727 registered users in 29 countries and now licensed to Coriell (January 2016). J.L. also reported the unfortunate recent withdrawal of Pluritest HT12 arrays and potential ways forward including the development of alternative DNA methylation or RNA analysis platforms. The preferred option appeared to be the development of a new platform based on RNAseq data (see RNA Skim method [15]). Prof. Loring outlined the options for total RNA or RNA exome analysis, of which the former was the currently preferred way forward as it would capture the lnc-RNAs used in the current Pluritest Platform.

Cell Differentiation on Plastic Microcarriers

Dr. Steve Oh (BTI, ASTAR) reported the development of a serum-free and chemically defined microcarrier-based suspension culture platform for scalable hPSC expansion and embryonic body (EB) formation. Improved survival and better quality embryoid bodies with the microcarrier-based method [16] resulted in significantly improved mesoderm induction and, when combined with hematopoietic differentiation, resulted in at least a sixfold improvement in hematopoietic precursor expansion. This culminated in an 80-fold improvement in the yield of red blood cells (RBCs) generation compared with a conventional EB-based differentiation method. In addition, he reported efficient terminal maturation and generation of mature enucleated RBCs using a coculture system that comprised primary human mesenchymal stromal cells. The microcarrier-based platform could prove to be an appealing strategy for future scale-up of hPSC culture, EB generation, and large-scale generation of RBCs under defined and xeno-free conditions.

Regulations and Informed Consent

A New ISO Standard for Biobanking

Dr. Tohru Masui (Keio University/SKIP, Yokahama, Japan) described the Stemcell Knowledge and Information Portal being developed in Japan (SKIP) as an international collaboration. Key challenges for SKIP included networking a variety of resources and the many potential identifiers for donors and cell lines. He summarized the ISO TC276 activity to establish a new international standard for biobanks and a new research project on its implementation for Japanese biobanks. ISCBI members perceived problems with the implementation of a very prescriptive TC276 single standard for all cell types and fed back constructive comments for a restructured document. The final international biobank standard (ISO20387) will be a framework standard for biobanks of various materials, including human, animal, plant, and microorganisms. Where adopted, it will require accreditation by assessment of competence of each biobank which will have financial implications, which could impact on research-based biobanks. However, the quality of biobank resources is crucial to facilitate effective research and development. Dr. Masui is coordinating a study group to set minimum criteria for biobanks with an achievable and realistic manner. In addition, he also described the Japanese ethics perspectives for ES cell research which are based on three principles to derive ES cells from donated human embryo which are have informed consent, voluntary donation, and complete anonymization. With the discovery of iPSC technology using somatic cells, many people thought that iPSCs avoided some of the ethical concerns about hESCs. However, it is clear that iPSCs require the same degree of traceability and anonymity. Accordingly, in 2013, Japan established three regenerative medicine related acts to address the challenges of these new advanced therapies. It will be tested at authorization and support at development of an innovative medical practice with iPSC.

Considerations on Ethics Issues for Use of Pluripotent Stem Cells

Dr. Geoff Lomax (CIRM, San Francisco, U.S.) summarized the general issues of concern at CIRM when establishing model informed consent procedures for donors of tissues used to create hPSC lines, which were (a) the potential for commercial development, (b) sensitive applications (e.g., creation of gametes and embryos, transplantation into humans), and (c) wide-ranging distribution and use of cells/derivatives and the associated genetic and medical information. Useful guidance had been established by the International Society for Biological and Environmental Resources, although this was primarily developed from a U.S. perspective. Key issues for users of hPSC lines were outlined as the impact of

withdrawal of consent, constraints on freedom to act commercially and constraints or regulation on the freedom to generate and use genetic data. Withdrawal of consent was an area of special concern which had been tackled in different ways in different jurisdictions. He explained that there had been cases where the stem cell line had been withdrawn when the donor withdrew consent and that it is vital to have clarity on whether the withdrawal of consent affects the cell line or just the original donated tissue sample. This clearly raised potential future problems that might be unsolvable once lines had been distributed by banks and issued clinically. CIRM considered a cut-off of passage 5 up to which all material could be retracted if consent were withdrawn. Consenting procedures should be clear on this issue as "silence" could raise doubts about the utility of lines in academia and industry. In other jurisdictions, only the original donor tissue could be withdrawn.

One of the key objectives of ISCBI is the development of best practices, which includes fostering harmonized or common approaches for determining sample/hPSC provenance as well as for developing and evaluating informed consent processes. Prof. Rosario Isasi (University of Miami, Miller School of Medicine, U.S.) mentioned ISCBI activities on analyzing policy convergence for prospective collection/derivation as well as for the utilization of previously collected specimens for hPSC derivation, banking, and distribution. There were discussions centered on identifying commonalities in the adoption of ethical safeguards to respect donors' autonomy (i.e., consent) and privacy interests (i.e., managing genetic data) and to ensure the ethical integrity of research as well. The ultimate goal is to ensure conformity with international ethical standards while respecting moral diversity and sovereignty as reflected in national regulatory frameworks.

Prof. Glyn Stacey (UKSCB, NIBSC, South Mimms, U.K.) described new data protection law in the EU which was an area of some concern to all delegates. The revisions to the EU Directive on Data Protection and its implementation in EU law could see significant additional controls on use of raw genetic data from hPSC lines. This will require screening and monitoring of all access to raw genetic data to ensure it is not misused and will affect any exchange of data derived from EU citizens. Such issues and the need for appropriate best practice for data management in bioresource centers were addressed for bio resources centers at a recent workshop [17].

Summary

In both of the above-mentioned ISCBI meetings, methods for quality control of genome integrity and stability have been considered and selection of appropriate assays for this aspect of quality control are still under investigation. The closely associated International Stem Cell Initiative (http://www.stem-cell-forum.net/) also organized a workshop on genetic stability (Jackson laboratories, Bar Harbor, October 2016, contributed to by ISCBI members), also addressed this issue and will publish its conclusions in 2017. Looking ahead, it will be important to recognize the difference between research-based characterization of genetic stability and the need for a cost-effective and standardized quality control assay for genome integrity in stem cell banks.

From the experiences of at least one of the regulatory bodies presenting at ISCBI meetings, it is apparent that the mesenchymal stromal cell (MSC) field has similar issues relating to culture stability and the need for screening of appropriate markers and functional assays. Similar discussions to those outlined here for hPSCs are therefore likely to be of benefit in the banking and control of MSC cultures. A number of groups are now developing hPSCs for clinical application using the ISCBI guidance which has also been taken up by banks now supplying hESCs specifically derived for use in human therapy. However, the ISCBI banking groups continue to discuss improvement in quality control for quality assurance, including characterization of stem cell lines. To this end, ISCBI meetings will continue to provide a forum for the evaluation of emerging technologies for culture, characterization, safety testing, and ethical guidelines. Such iterative processes between expert centers will be important in the establishment of safe and effective stocks of stem cells for future regenerative medicines.

Notwithstanding developments in cell safety and efficacy, issues for managing ethical aspects of both hESC and iPSC remain challenging with increasing regulation to be addressed for any derivatives of human tissues. Standardization in the delivery of stem cell biobanking and cell therapy products is also progressing, and those developing and supplying stem cell lines for clinical application will need to keep abreast of new developments and emerging issues. It is therefore vital that groups like the ISCBI continue to stimulate exchange of information on international developments and review best practice in stem cell banking on a regular basis. The ISCBI community will continue to provide a forum for such discussions among key stakeholders including bioresource centers, stem cell biologists, regulators, and others with crucial complementary expertise.

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Author Contributions

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Disclosure of Potential Conflicts of Interest

N.R. is an employee of Neurona Therapeutics. T.J.N. is an employee of Cellular Dynamics International. The other authors indicated no potential conflicts of interest.

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